Remarks

Rule 132 Declaration

A declaration of Dr. Timofei Nikita Kroupenkine under the provisions of 37 CFR §1.132 accompanies this response. Hereinafter references to Dr. Kroupenkine's declaration will be cited as [***Kroupenkine***] with appropriate paragraph designations.

Amendments

Independent claim 1 has been amended, without prejudice, to correct a grammatical error.

Dependent claims 9 and 19 have been amended, without prejudice, to improve their clarity; that is, to particularly point and distinctly claim that the first and second zones are laterally separate and electrically isolated from one another.

It is respectfully submitted that no new matter has been added.

Summary of the Invention

Before discussing the rejection on the merits, it will be helpful to briefly review Applicants' invention.

In one aspect of the invention, as set forth in both independent claims 1 and 18, a stent comprises a tubular member having an interior surface and an exterior surface, with a region of at least one of the ***surfaces*** being ***hydrophobic***; that is, the surface has a contact angle greater than 90°. The ***hydrophobic surface*** region is provided with an array of microstructures or nanostructures that covers first portions of the surface but leaves second portions exposed in the interstices of the array. These structures cause the region to have a ***dynamically controllable*** hydrophobicity.

In one embodiment, a control device, which is affixed to the tubular member, varies the surface hydrophobicity of the region (claim 2; claim 18, lines 29 ***et seq.***). In another embodiment, which is particularly applicable to the delivery of a medicinal substance (e.g., a chemically active agent such as pharmacological agent or drug) to fluids in body vessels, the stent also includes such a medicinal substance that adheres to the exposed portions until the

control device alters the hydrophobicity of the region and causes the substance to be released into the body fluid in contact with the stent (claims 5-7; claim 18, lines 29 ***et seq.***). In still another embodiment, the control device is remotely actuated from a source located external to the body (claim 4; claim 18, page 5, line 2).

In still another aspect of the invention, the hydrophobic surface region is ***tiled***; that is, divided into at least first and second electrically isolated zones whose surface hydrophobicity is separately controllable, so that, for example, chemically active (e.g., medicinal) substances adhered to those zones may be selectively released (claim 9; claim 19). The same substances, with the same or different dose, may be adhered to the first and second zones (claim 10; claim 20), or different substances may be adhered to the first and second zones (claim 11; claim 21).

Claim Rejections – Issues in Common

Many of the claim rejections discussed below have several issues in common including: (1) the standard definition of hydrophobic, (2) a purported "special definition" of hydrophobic adopted by Applicants; (3) the alleged hydrophobic nature of metals; and (4) alleged product-by-process limitations in the claims. Issues (1) and (3) are raised, in part, by the following statements made by the Examiner:

> Please note that the Examiner is interpreting hydrophobic according to a known, common definition. ***According to Dorland's Illustrated Medical Dictionary (2003) hydrophobic is defined as: not readily absorbing water***. Thus, since it is known metals do not absorb water, the surface of [the prior art stent] must be hydrophobic. The surface is fully capable of having hydrophobicity that has a contact angle greater than 90° when a drop of fluid contacts it. (italics in the original)

This dictionary will hereinafter be referred to as ***Dorland.***

Issue (1): The standard, well-known definition of ***hydrophobicity*** is correctly stated in the previously-cited article from ***Wikipedia*** [***Kroupenkine***, paragraph 5]. The article begins by describing the phenomenon of wetting as the "contact between a liquid and a solid surface." From the standpoint of fundamental surface physics, the article also states correctly that the "degree of wetting is described by the contact angle" and that a "contact angle of 90° or greater generally characterizes a surface as not-wettable, and one less than 90° as wettable. In the

context of water, the article states that "a wettable surface may also be termed ***hydrophilic*** and a not-wettable surface ***hydrophobic***." This statement is correct for aqueous liquids in general. Thus, the article clearly and correctly teaches that a hydrophobic surface is not wettable and, therefore, has a contact angle greater than 90° to a water droplet (Figure 1). Applicants' use of the term follows this standard definition; that is, Applicants' specification (page 5, line 21) explicitly states that a hydrophobic surface is "a low-energy surface that is characterized by a high contact angle (> 90°) to any body fluid it contacts." (This limitation is explicit in independent claims 1 and 18.) Since it is notoriously well known that body fluids, such as blood, are aqueous, it follows that the standard definition of ***hydrophobic*** is equally applicable to Applicants' invention and is essentially identical with the explicit definition given in Applicants' specification [***Kroupenkine***, paragraph 5].

In contrast, ***Dorland's*** definition describes a ***necessary but not sufficient*** condition that is inherent in any hydrophobic surface; that is, the surface does not absorb water [***Kroupenkine***, paragraph 7]. But, the ***Dorland*** definition is incomplete because it fails to consider the critical nature of ***adsorption***, particularly the interaction between water and a hydrophobic surface. In standard surface physics that interaction is defined in terms of the contact angle between the hydrophobic surface and a water droplet (cf., Figure 1, ***Wikipedia***). The missing aspects of the ***Dorland*** definition are particularly important because Applicants' invention is predicted on the use of a microstructured or nanostructured surface to dynamically control the hydrophobicity of that surface. (Hereinafter, for simplicity Applicant will refer to the surface as being nanostructured.) In one important embodiment of Applicants' invention, this dynamic control involves the application of suitable voltages to the stent, which allows a pharmacological agent or a drug to be alternately captured by or released by the nanostructured stent surface.

Issue (2): In addition, at page 8 of his "Response to Arguments" (Final Office Action of May 8, 2008) the Examiner asserts, without proper support, that Applicants have adopted a "special definition" of hydrophobic. In addition, the Examiner also asserts that "the limitation of 'a contact angle greater than 90° when a fluid contacts the surface' is a description of the characteristics of a treated surface, it is not the definition of 'hydrophobic." To the contrary, as Dr. Kroupenkine's declaration demonstrates, Applicants' definition of hydrophobic is the

standard definition well known in the physics art used to analyze the interaction between liquids and the surface of a solid. This definition is soundly based in surface physics applicable to the art of Applicants' invention [***Kroupenkine***, paragraph 5]. In contrast, ***Dorland's*** definition is incomplete [***Kroupenkine***, paragraph 7].

Issue (3): It is respectfully submitted that the Examiner's position on metals is also fallacious; that is, the Examiner's position, as reflected by the notion that metals don't absorb; therefore, metals must be hydrophobic, is simply incorrect. First, this argument contravenes the standard definition of hydrophobicity, as discussed above. Second, the prior art teaches that the contact angles of illustrative clean metal surfaces are ***hydrophilic, not hydrophobic***; that is, they have contact angles less than 90° (Au ~ 71°; Pt ~ 0°; stainless steel < 5°). Thus, the Examiner's ***unsupported assumption*** is without foundation in the art. Moreover, the further assumption that "[any metal] surface is ***fully capable*** of having a hydrophobicity that has a contact angle greater than 90°" is not supported by the prior art (emphasis added) [***Kroupenkine***, paragraph 9].

Issue (4) Claims 1 and 18 contain the limitation "at least one of said [tubular member] surfaces being hydrophobic to a body fluid in that the contact angle between a droplet of said fluid and said at least one surface is greater than 90°." The Examiner asserts that this claim limitation "is considered as a ***product-by-process*** limitation and that the product itself does not depend on the process of for making it (emphasis added)." To the contrary, the statement that a surface has contact angle greater than 90° describes a characteristic of the surface itself, not a process step for making a stent [***Kroupenkine***, paragraph 11]. Accordingly, it is respectfully submitted that the Examiner has misinterpreted the facts and misapplied the law in this regard. Full patentable weight should, therefore, be given the contact angle limitation of Applicants' claims.

Claim Rejections – 35 USC §102 and §103

Claims 1-8, 12-13 and 18-20 have been rejected under 35 USC §102(b) as being anticipated by or, in the alternative, under 35 USC §103(a) as obvious over S. R. Bailey ***et al.***, International Application Publication No. WO 02/064019, which was published on August 22, 2002 (hereinafter ***Bailey***).

Claims 1-2, 5-7 and 9-11 have been rejected under 35 USC §102(e) as being anticipated by or, in the alternative, under 35 USC §103(a) as obvious over C. Momma ***et al.***, US Patent Application Publication No. 2005/0027350, which was published on February 3, 2005 based on an application filed on July 30, 2003 (hereinafter ***Momma***).

Claims 1-2, 5-7 and 15-17 have been rejected under 35 USC §102(e) as being anticipated by or, in the alternative, under 35 USC §103(a) as obvious over V. P. Shastri ***et al.***, US Patent Application Publication No. 2004/0115239, which was published on July 17, 2004 based on an application filed on September 22, 2003 (hereinafter ***Shastri***).

Claims 1 and 14 have been rejected under 35 USC §102(b) as being anticipated by or, in the alternative, under 35 USC §103(a) as obvious over H. S. Oktay, US Patent Application Publication No. 2003/0040791, which was published on February 27, 2003 based on an application filed on August 22, 2002 (hereinafter ***Oktay***).

These rejections are respectfully traversed for ***any one or more*** of the reasons set forth below.

(1) **Anticipation:** The law of anticipation under Section 102 is clear, as set forth in MPEP 2131: "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ...claim." *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). ***Each and every element*** of Applicants' claims is ***not*** found in either Bailey, or Momma, or Shastri, or Oktay, as discussed below.

(2) **Surface Hydrophobicity-Standard Definition:** The standard, well known definition of ***hydrophobicity*** is illustrated in the attached article from ***Wikipedia***, which describes the phenomenon of ***wetting*** as the "contact between a liquid and a solid surface." The article also states that the "degree of wetting is described by the contact angle" and that a "contact angle of 90° or greater generally characterizes a surface as not-wettable, and one less than 90° as wettable. In the context of water, a wettable surface may also be termed ***hydrophilic*** and a not-wettable surface ***hydrophobic***."

Thus, the article clearly and correctly teaches that a hydrophobic surface is not wettable and, therefore, has a contact angle greater than 90° to water. Applicants' use of the term follows this standard definition; that is, Applicants' specification (page 5, line 21) explicitly states that a hydrophobic surface is "a low-energy surface that is characterized by a high contact angle (> 90°) to any body fluid it contacts." (This limitation is explicit in independent claims 1 and 18.) Since it is notoriously well known that body fluids, such as blood, are aqueous, it follows that the standard definition of ***hydrophobic*** is equally applicable to Applicants' invention [***Kroupenkine***, paragraph 5].

(3) **Surface Hydrophobicity-Examiner's Definition:** As noted above, the Examiner asserts, without support, that Applicants have adopted a "special definition" of hydrophobic. To the contrary, Applicants' definition of hydrophobic is consistent with the standard definition well known in the art. [***Kroupenkine***, paragraph 8] Instead, he attempts to imbue a set of references, which are ***silent*** on the matter of hydrophobicity, with an unsupported notion that they inherently "disclose materials for the stent surfaces that clearly have a low affinity for water or are ***in other words hydrophobic***." The Examiner continues this fallacious argument by asserting that the failure of stent materials (mostly metals) to ***absorb*** body fluids somehow makes them hydrophobic [***Kroupenkine***, paragraph 9]. However, as discussed above, lack of absorption is a necessary but ***not*** sufficient condition of the definition; having a contact angle greater than 90° defines makes a surface hydrophobic (claims 1 and 18) [***Kroupenkine***, paragraph 5].

(4) **Surface Hydrophobicity-Metals:** The Examiner's position on Bailey, Momma and Oktay typifies his position; to wit, metals don't absorb; therefore, metals must be hydrophobic. This argument contravenes the standard definition of hydrophobicity, as discussed in above. Second, the prior art teaches that the contact angles of illustrative clean metal surfaces are hydrophilic, not hydrophobic; that is, they have contact angles less than 90° (Au ~ 71°; Pt ~ 0°; stainless steel < 5°). Thus, the Examiner's ***unsupported assumption*** is without foundation in the art [***Kroupenkine***,

paragraph 9].

(5) **Dynamically Controllable Hydrophobicity-General:** Applicants' invention requires that the surface hydrophobicity is ***dynamically controlled*** (claim 1, lines 7-8; claim 18, lines 23-24). To this end, various embodiments of Applicants' invention include an array of nanostructures (claim 1, lines 6-7; claim 18, lines 22-23) in a first portion of the surface and a control device affixed to the tubular member for varying the hydrophobicity (claim 2; claim 7; claim 18, lines 29 ***et seq.***). Even assuming, ***arguendo***, that the references relate to surface hydrophobicity, none describes the dynamic control of that hydrophobicity.

(6) **Dynamically Controllable Hydrophobicity-Specific:** In a preferred embodiment of Applicants' invention, as set forth in claim 18, a combination of additional novel features gives rise to patentability, including: (i) an array of ***pillar-like*** nanostructures (claim 18, lines 22-23); (ii) dynamically controllable hydrophobicity between a first state, in which the body fluid is suspended over the top of the nanostructures, and a second state, in which the fluid penetrates the interstices of the nanostructures (claim 18, lines 24-26); (iii) a medicinal substance located in the interstices (claim 18, lines 27-28); and (iv) a control device causing the release of the medicinal substance when in the second state (claim 18, page 2, lines 1-2). This combination of features is neither taught nor suggested by the art of record. Therefore, claim 18, and claims 19-21, which depend therefrom, are patentable not only by virtue of their inclusion of a hydrophobic surface, as discussed in paragraphs (2)-(5) above, but also because of the specifically-defined control of that hydrophobicity, as discussed in this paragraph.

(7) **Dynamically Controllable Hydrophobicity-Bailey:** In Bailey, the Examiner states "Another stent is also disclosed that describes an array of microstructures or grooves and hydrophobicity can be controlled in a dynamic fashion, page 10, lines 17-33. The cellular response and its effect on the microstructure clearly effects (***sic***) hydrophobicity." However, this section of Bailey merely describes an endoluminal implant having a plurality of microgrooves on the luminal and/or abluminal surfaces thereof which facilitate improved endothelialization over a non-grooved implant. The

Examiner's bald assertion that these grooves and/or the cellular response to them "clearly effects (*sic*) hydrophobicity" is pure speculation. Bailey does not describe a hydrophobic surface; nor is such a surface inherent in his device. In addition, even assuming, ***arguendo***, that a hydrophobic surface were present, Bailey fails to teach that the grooves would be used to dynamically control such hydrophobicity. No such control is described.

(8) **Electrically Isolated Zones:** Regarding Bailey, the Examiner asserts that the limitation of dependent claim 19 that the exposed second surface includes "isolates zones" is an "arbitrary limitation." But, the Examiner conveniently igores the fact that original claim 19, as well as amended claim 19, require that these zones are ***electrically isolated*** from one another. Nothing in Bailey even remotely teaches or suggests this feature. In this regard, see also paragraph (13), ***infra***.

(9) **Variable Penetration of Interstices:** Claim 8 calls for a control device that varies the "penetration of the interstices of said array by said fluid, thereby causing release of said agent or drug into said fluid." Claim 18 has a similar requirement at lines 24-26. This feature has not been adequately addressed by the Examiner in his rejection of claims 8 and 18 in view of Bailey. Instead, the Examiner merely offers an unsupported conclusion that Bailey's "fluid is capable of being suspended over the microstructures in a first state and then penetrate between the microstructures in a second state." This feature is not even remotely taught or suggested by Bailey. Consequently, a ***prima facie*** case of anticipation has not been established. In summary, Bailey is totally devoid of any teaching of this control feature, which enables Applicants' array to control surface hydrophobicity and, in turn, the release of agents/drugs located in the interstices.

(10) **Dynamically Controllable Hydrophobicity-Momma:** The Examiner asserts that FIG. 2 of Momma "shows a stent body 42 that includes an array (*sic*) microstructures 38 and control device in the form of a membrane 46 to vary hydrophobicity." First, contrary to the Examiner's unsupported assertion, the mere fact that Momma's stent is a metal does not make the metal surface hydrophobic [***Kroupenkine***, paragraphs 6,

7 and 9]. Second, even assuming, ***arguendo***, that a hydrophobic surface were present, there is no evidence that Momma's array of raised micro-channels 38 would affect surface hydrophobicity in the fashion claimed. Third, element 46 is merely a biodegradable cover layer that releases underlying active substance 44 into blood vessel media 22. Momma provides no teaching that cover layer 46 has any effect, no less control, of surface hydrophobicity, as required by claim 1.

(11) **Dynamically Controllable Hydrophobicity-Shastri:** The Examiner points to Shastri's disclosure that "fibers or particles of nanosize" are "placed on the surface of an implant" and chemically active substances can be used on the device with control devices (polymer materials). These [control devices?] "include cells that change the surface properties or hydrophobicity." Then, the Examiner concludes that "Shastri discloses (paragraph 87) properties modified or controlled, including wettability that the Examiner interprets to be synonymous with hydrophobicity." First, Shastri fails to teach a hydrophobic surface, as discussed above. Second, the Examiner's interpretation that "wettability [is] synonymous with hydrophobicity" is contrary to the standard definition of these terms, as discussed in Dr. Kroupenkine's declaration. Third, even assuming, ***arguendo***, the presence of a hydrophobic surface, there is no evidence that Shastri's particles and/or cells affect surface hydrophobicity. Fourth, the Examiner references paragraphs 75, 79, 82 and 84 of Shastri to show that "chemically active substances can be used on the devices with control devices (polymer materials)," but there is no evidence in these paragraphs that any such device controls the surface hydrophobicity of Shastri's deposited particle layer.

(12) **Dynamically Controllable Hydrophobicity-Oktay:** The Examiner asserts that Oktay's FIG. 10 shows "a stent 1000 with an array of microstructures 1050, 1060 on a region of the stent." However, the elements 1050, 1060 are, in fact, MEMS motors, not "microstructures," as that term in used in Applicants' claims, capable of controlling hydrophobicity. Next, the Examiner asserts that "Oktay discloses (paragraph 69) the stent structure is made of metal and ***thus is hydrophobic.*** As discussed above, however, the Examiner's logic fails when tested in the light of the

standard definition of hydrophobic and the known ***hydrophilic*** nature of metals [***Kroupenkine***, paragraphs 6, 7 and 9].

(13) **Tiled Hydrophobic Surface:** Claims 9 and 19 recite a stent design in which the array of nanostructures covers first portions of the stent surface, and second portions (e.g., the interstices of the array) remain exposed. This exposed portion is ***tiled*** in this embodiment of the invention; that is, divided into laterally separate, ***electrically isolated*** first and second zones, which have chemically active substances adhered thereto. The control device actuates the release of the substances from the zones. In this regard, the Examiner has cited Bailey against claim 19 and Momma against claim 9. However, in applying Bailey to claim 19, the Examiner does not properly address the separate control of tiled, laterally separate, electrically isolated surface zones leading to the controlled release of substances from predetermined zones. Thus, a ***prima facie*** case of anticipation of claim 19 in view of Bailey has not been made out. Likewise, what Momma teaches in this regard is quite different from Applicants' invention, as defined by claim 9. Momma's approach to the release of multiple, different substances is evident from FIG. 2, which shows two active substances 52, 54 ***stacked*** on top of one another at the ***same*** implantation site. The upper active substance 54 is covered by a biodegradable layer 46, and the lower active substance 52 is covered by a biodegradable layer 50, which also separates the two active substance layers 52, 54 from one another. Over time the upper cover layer 46 biodegrades releasing upper active substance 54. Later, the lower cover layer 50 biodegrades releasing lower active substance 52. Note, the biodegradation of cover layers 46, 50 is a ***passive*** function; it not ***dynamically*** controlled by an ***ex vivo*** source as required by claim 9. In addition, claim 9 requires that the ***exposed portion of the hydrophobic surface is electrically isolated into laterally separate, first and second spatial zones*** containing a chemically active substance (i.e., the surface is ***tiled*** into separately controllable zones), and the control device is capable of causing separate release of the substances from the first and second zones at different times. Clearly, for each micro channel 38 Momma's stacked, active substances are disposed in/above

the ***same zone of the surface***, not in ***different*** surface zones, and Momma's control of the release of the substances is passive not dynamic.

In view of the foregoing it is respectfully submitted that claims 1-20 are not anticipated by Bailey, Momma, Shastri or Oktay.

Claim Rejections – 35 USC §103

Associated with each of the foregoing rejections of claims 1-20 under 35 USC §102 there is an alternative rejection under 35 USC §103(a). The Examiner admits that Bailey, Momma, Shastri and Oktay do not explicitly state the [stent] surface has a contact angle greater than 90° when any drop of fluid contacts it," but then improperly dismisses the corresponding feature of Applicants' claims as a "product by process" limitation. This statement is patently incorrect as a matter of fact [***Kroupenkine***, paragraph 11]. Moreover, the conclusion that it would have been obvious matter of routine skill to include this feature in the prior art stents is incorrect as a matter of law; it is clearly an improper attempt to use hindsight and Applicants' own teaching conjure up a feature not disclosed in the references and, thereby, to render Applicants' claims obvious.

Accordingly, it is respectfully submitted that each of Bailey, Momma, Shastri and Oktay fail to render obvious Applicants' invention as defined by claims 1-20.

In addition, claim 21 has been rejected under 35 USC §103(a) as being unpatentable over Bailey in view of Momma. However, this rejection is predicated on the notion that all of the limitations of independent claim 21 are taught by Bailey except for "different substances to be released into the implantation site."

This rejection is respectfully traversed. Note, first, that claim 21 depends from claim 18. Second, as argued in paragraph (7) above with reference to the Section 102 rejections based on Bailey, which arguments are incorporated herein by reference, claim 18 includes several fundamental, patentably distinguishing features (including those related to the dynamic control of surface hydrophobicity) that are not disclosed by Bailey. Moreover, these deficiencies are not remedied by Momma. Accordingly, claim 21, which depends from claim 18, is likewise patentable.

In addition, however, even assuming, ***arguendo***, that the Examiner's position on Bailey is correct, his further reliance on Momma is misplaced. More specifically, the Examiner makes the following assertions:

> Momma et al. teach different medicinal substances can be utilized to deliver to the implantation site for different purposes, paragraphs 21, 45. It would have been obvious...to incorporate different drugs on the stent as taught by Momma et al. in the stent of Bailey...

What Momma teaches in this regard, however, is quite different from Applicants' invention. Momma's approach to the release of multiple, different substances is evident from FIG. 2, which shows two active substances 52, 54 ***stacked*** on top of one another at the ***same*** implantation site. The upper active substance 54 is covered by a biodegradable layer 46, and the lower active substance 52 is covered by a biodegradable layer 50, which also separates the two active substance layers 52, 54 from one another. Over time the upper cover layer 46 biodegrades releasing upper active substance 54. Later, the lower cover layer 50 biodegrades releasing lower active substance 52. Note, the biodegradation of cover layers 46, 50 is a ***passive*** function; it not ***dynamically*** controlled by an ***ex vivo*** source as required by claim 18, line 19. In addition, claims 18-19, from which claim 21 depends, require that the ***exposed portion of the hydrophobic surface is electrically isolated into first and second spatial zones*** containing a medicinal substance (i.e., the surface is ***tiled*** into separately controllable zones), and the control device is capable of causing separate release of the substances from the first and second zones (claim 19). Claims 21 requires that the medicinal substances adhered to the first and second surface zones are different substances. Clearly, for each micro-channel 38 Momma's stacked, active substances are disposed in/above the ***same zone of the surface***, not in ***different*** surface zones, and Momma's control of the release of the substances is passive not dynamic.

Accordingly, it is respectfully submitted that the combination of Bailey and Momma fail to render obvious Applicants' invention as defined by claim 21.

Conclusion

In view of the foregoing, reconsideration of claims 1-21, and passage of this application to issue, are hereby respectfully requested. If during the consideration of this paper, the Examiner believes that resolution of the issues raised will be facilitated by further discussion, she is urged to contact the undersigned attorney at 610-691-7710 (voice) or 610-691-8434 (fax).

Respectfully,

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